K093815

MAR 12 2010

510(k) SUMMARY

Submitter: Millipore Corporation
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Contact Name: Catherine Karaman

Date Prepared: November 19, 2009

Product Name

Trade Name: *Light Diagnostics*™ Human Metapneumovirus DFA Kit
Common Name: Immunofluorescence Assay
Classification Name: Human Metapneumovirus - unclassified

Intended Use

***Light Diagnostics*™ Human Metapneumovirus DFA Kit** is intended for the detection and identification of human metapneumovirus (hMPV) in direct respiratory specimen cell preparations from nasopharyngeal swabs from patients with febrile respiratory illness. This assay detects but is not intended to differentiate the four recognized genetic sub-lineages of hMPV.

Negative results do not preclude hMPV infection and should not be used as the sole basis for diagnosis, treatment or other management decisions. It is recommended that specimens found to be negative after examination of the direct specimen results be confirmed by FDA cleared hMPV molecular assay.

For In Vitro Diagnostic Use.

Predicate Device

1) Validated RT-PCR method followed by bi-directional sequencing for confirmation and identification of Human Metapneumovirus

Device Description

Light Diagnostics Human Metapneumovirus DFA Kit utilizes a single reagent for the detection and identification of human metapneumovirus. The fluorescein labeled monoclonal antibodies, specific for human metapneumovirus will bind to viral antigen in human metapneumovirus infected cells. Unbound reagent is removed by rinsing with phosphate-buffered saline (PBS/Tween 20). Illumination allows visualization of the antigen-antibody complex by fluorescence microscopy. When a FITC filter set is used, the human metapneumovirus antigen-antibody complex will exhibit an apple-green fluorescence. Uninfected cells stain a dull red due to the presence of Evans blue in the reagent.

Technological Comparison of Methods

Comparison with Predicate:

During this study no FDA cleared predicate device was available. The performance characteristics of the Light Diagnostics™ Human Metapneumovirus DFA Assay were established by direct evaluation of clinical specimens compared to a composite algorithm based on cell culture results and a validated RT-PCR method followed by bidirectional sequencing for confirmation and identification of human metapneumovirus.

The methods differ in that:

Light Diagnostics™ Human Metapneumovirus DFA Kit contains a single reagent which contains FITC-labeled monoclonal antibodies directed against hMPV. This reagent detects hMPV antigens present in the patient specimen. Slides are necessary to detect and identify the virus from sample and yield an apple-green fluorescence color if positive. The composite RT-PCR/sequencing method detects viral RNA isolated from patient specimens.

1) Analytical Performance:

Cross-reactivity against common viruses, bacteria, and cell lines

The monoclonal antibodies used in the Light Diagnostics™ hMPV Direct Immunofluorescence Assay **hMPV** Reagent were tested against a variety of viruses and bacteria found in the respiratory tract, and cell lines commonly used to isolate respiratory viruses. Bacteria were tested with 10^6 CFU and viruses with 10^5 PFU/ml. No cross-reactivity was observed for the hMPV Reagent when tested with the specified viruses, bacteria, or cell lines. The results are indicated in the table below.

Organism or	hMPV Reagent
Adenovirus	Negative
Cytomegalovirus (CMV)	Negative
Herpes simplex virus, type 1 (HSV-1)	Negative
Herpes simplex virus, type 2 (HSV-2)	Negative
Influenza A virus	Negative
Influenza B virus	Negative
Parainfluenza virus type 1	Negative
Parainfluenza virus type 2	Negative
Parainfluenza virus type 3	Negative
Respiratory syncytial virus (RSV)	Negative
Varicella-zoster virus (VZV)	Negative
Escherichia coli	Negative
Hemophilus influenzae	Negative
Moraxella catarrhalis	Negative
Pseudomonas aeruginosa	Negative
Staphylococcus aureus	Negative
Staphylococcus epidermis	Negative
Streptococcus pyogenes	Negative
Streptococcus salivarius	Negative
Cell Lines	
A549	Negative
BGMK	Negative
Hep-2	Negative
LLCMK2	Negative
MDCK	Negative
MRC-5	Negative
RD	Negative
Vero	Negative

Analytical Reactivity

In addition to the Analytical Sensitivity results (see below) a study was performed to demonstrate that the Light Diagnostics™ hMPV DFA Reagent detects virus isolates representing each of the four known genetic sublineages of hMPV (A1, A2, B1, B2). Positive specimens from the clinical study were genotyped to further support this study. The Light Diagnostics™ hMPV DFA Reagent detected hMPV in 21 clinical isolates from sublineage A2, 10 from sublineage B1, and 32 from sublineage B2 (including positive specimens from Site Three).

Virus subtypes	hMPV Reagent
hMPV A1	+
hMPV A2	+
hMPV B1	+
hMPV B2	+

Precision/Reproducibility

Precision/reproducibility studies were conducted using the Light Diagnostics™ hMPV DFA Reagent at three testing sites (one internal and two external) using multiple operators, multiple runs per day and multiple viral concentrations of a test panel. The test panel consisted of one true negative sample and samples at three levels of viral load including a high negative (sample with an analyte concentration below the LoD such that repeat testing of this sample should be negative at least 95% of the time), a low positive sample, and a moderate positive sample.. In internal testing, results were 100% in accordance with expected results (80/80 tests). In external testing, results were in accordance with expected results greater than 99% of the time (438/440 tests). The results of both external and internal testing are summarized below.

Number of Operators	Number of Sites	Viral control level	Expected Results	Results	%Accordance with expected results
4	2	Moderate	Positive	Positive 90/90	100%
6	3	Low	Positive	Positive 130/130	100%
4	2	High Negative (viral concentration below Limit of Detection)	Negative	Negative 88/90 Positive 2/90	97%
6	3	Uninfected	Negative	Negative 130/130	100%
			Overall	438/440	99%

Analytical Sensitivity (Limit of Detection)

The Light Diagnostics™ hMPV DFA Reagent was tested with slides made from titrated quantitated virus culture. Four strains of hMPV were used, representing all four known subtypes of hMPV. Five ten-fold dilutions were made from viral seed stocks of known concentration for each strain. Samples of virus at each dilution were dropped on slides in

duplicate, and four batches of slides were prepared from four cultures (eight replicates at each concentration). Positive results were obtained with at least 95% of replicates using the Light Diagnostics™ hMPV DFA Reagent on hMPV A1 infected cells down to 400 PFU/mL, 100 PFU/mL of hMPV A2 infected cells, 625 PFU/mL of hMPV B1 infected cells, and 275 PFU/mL of hMPV B2 infected cells. Results are summarized below.

Virus strain	Limit of Detection
hMPV A1	4.0×10^2 PFU/mL
hMPV A2	1.0×10^2 PFU/mL
hMPV B1	6.25×10^2 PFU/mL
hMPV B2	2.75×10^2 PFU/mL

2) Clinical Evaluation:

Clinical samples were submitted to each clinical laboratory in viral transport media, the cells were washed in PBS, dropped onto slides, and fixed in acetone. Slides were stained with the Light Diagnostics™ Human Metapneumovirus DFA Kit and examined using fluorescence microscopy. Clinical samples were also analyzed by a composite algorithm based on culture/RT-PCR/sequencing.

In the clinical study, nasopharyngeal swabs were the most prevalent specimen type.

At Site One, 208 nasopharyngeal swab specimens were submitted to a regional medical center in southeastern Canada for hMPV testing. At Site Two, 199 nasopharyngeal swab specimens were submitted to a hospital laboratory in the northeastern United States for hMPV testing. At Site Three 200 specimens were submitted for testing, of which four were nasopharyngeal swabs. The total combined number of NPS specimens was 411. Sixty-Three specimens were found positive for hMPV by RT-PCR. Of these, the Light Diagnostics Direct Immunofluorescence Assay detected 58 hMPV positive specimens. Analysis for sensitivity, specificity, positive and negative predictive values are given below.

Detection of hMPV in Direct Specimens using Light Diagnostics™ Human Metapneumovirus DFA Kit vs. RT-PCR

DETECTING hMPV		RT-PCR		
		Positive	**Negative**	**Total**
Light Diagnostics™ Human Metapneumovirus DFA Kit on direct specimens	**Positive**	58	2	60
	Negative	5	346	351
	Total	63	348	411
		95% Confidence Interval		
Sensitivity	92%	83-97%		
Specificity	99%	98-100%		
Positive Predictive Value	97%	89-99%		
Negative Predictive Value	99%	97-99%		

Conclusions Drawn from Evaluation:

Light Diagnostics™ Human Metapneumovirus DFA Kit uses a standard direct immunofluorescence assay procedure for the direct detection of hMPV in nasopharyngeal swab patient specimens. The monoclonal antibodies used in the reagent have been characterized to ensure specificity and reliability of the product. In clinical evaluations, the performance characteristics of the reagents were shown to be substantially equivalent to the predicate device.

The characterization and clinical evaluation of the **Light Diagnostics™ Human Metapneumovirus DFA Kit** demonstrates it is substantially equivalent to the predicate when used as intended as described in the product insert.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
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Document Mail Center-WO66-G609
Silver Spring, MD 20993-0002

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Millipore Corporation
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Clinical and Regulatory Affairs Specialist
28820 Single Oak Drive
Temecula, CA, 92590

Re: k093815

Trade/Device Name:	Light Diagnostics™ Human Metapneumovirus Direct Immunofluorescence Assay
Regulation Number:	21CFR §866.3980
Regulation Name:	Respiratory Viral Panel Multiplex Nucleic Acid Assay
Regulatory Class:	Class II
Product Code:	OMG
Dated:	December 7, 2009
Received:	December 14, 2009

Dear Ms. Karaman:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must

comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050. This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indication for Use

510(k) Number (if known): ____K093815_____

Device Name: Light Diagnostics™ Human Metapneumovirus DFA Kit

Indication for Use:

***Light Diagnostics*™ Human Metapneumovirus Direct Immunofluorescence Assay** is intended for qualitative detection and identification of human metapneumovirus (hMPV) in direct respiratory specimen cell preparations from nasopharyngeal swab samples collected from patients with febrile respiratory illness. This assay detects but is not intended to differentiate the four recognized genetic sub-lineages of hMPV.

Negative results do not preclude hMPV infection and should not be used as the sole basis for diagnosis, treatment or other management decisions. It is recommended that specimens found to be negative after examination of the direct specimen results be confirmed by FDA cleared hMPV molecular assay.

For *in vitro* diagnostic use.

Prescription Use ___√___ And/Or Over the Counter Use ____
(21 CFR Part 801 Subpart D) (21 CFR Part 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE; CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety

510(k): K093815